REMARKS

Claims 35-41, 47-50, 55-61, 67-69, 75-78, 80-82 and 86-90 are pending. Claims 1-34, 42-46, 51-54, 62-66, 70-74, 79 and 83-85 have been canceled without prejudice. Applicants reserve the right to pursue the subject matter of any canceled or amended claim, or any other unclaimed subject matter in one or more divisional, continuation or continuation-in-part applications.

Claims 35, 39-41, 47, 48, 55, 59-61, 67, 68 and 78 have been amended to be in independent format. A more detailed discussion is set forth below in Section III.

Claims 36-38, 50, 56-58, 69, 75-77 and 80-82 have been amended to change the claim(s) from which each depends.

Claim 50 has been further amended correct a typographical error and to more clearly set forth the claimed invention.

Claim 80 has been further amended to recite certain groups for the variable -A-R_1.

Claims 81 and 82 have been further amended to recite certain groups for the variable R_2.

Claims 86 and 87 have been amended to correct an error wherein the groups represented by the variable R_4 were inadvertently left out of the claims. Support for these amendments is found in the specification as filed at least at page 10, lines 1-3.

New claims 88-90 have been added. Support for new claims 88-90 is found in the specification at page 7, lines 13-15.

No new matter has been added.

A brief discussion of the claimed invention is helpful prior to addressing the rejections. The application is a divisional of U.S. application No. 09/910,950, filed July 23, 2001, now U.S. Patent No. 6,897,231, issued May 24, 2005, which is directed to novel compounds that have pharmaceutical utility. Applicants have amended the claims presented herein to the use of the compounds in the issued claims of the parent case. Thus, the claimed invention encompasses specific uses of a specific class of compounds, which compounds have already been determined to be novel and non-obvious. Indeed, the invention is thus tailored and, as discussed below, is not "extremely complex" and broad.

I. The Rejection of Claims 22-24, 75-84, 86 and 87 Under 35 U.S.C. § 112, First Paragraph

Claims 22-24, 75-84, 86 and 87 have been rejected under 35 U.S.C. § 112, first paragraph, for allegedly not providing enablement for the treatment of the term "cancer." In particular, while acknowledging that the specification is enabling for the treatment of specific cancers (*e.g.*, lung cancer), the Examiner has stated that the specification is not enabling for the treatment of any or all cancers. Applicants respectfully disagree.

The test for enablement is whether or not any person skilled in the art could make and use the invention from the disclosure in an application, coupled with information known in the art, without undue experimentation. *U.S. v. Telectronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir. 1988). The Federal Circuit has held that a specification which contains a teaching of how to make and use an invention is presumed to comply with the enablement requirement unless there is some reason to doubt the objective truth of the statements relied on for enabling support. *Fiers v. Revel*, 984 F.2d 1164, 1171-72 (Fed. Cir. 1993). Applicants submit that the present specification teaches how to make the compounds recited in the present method claims (at least at pages 15-26 and Examples 1-430, at pages 35-396), teaches how to prepare the compounds for pharmaceutical administration (*i.e.*, compositions and dosages suitable for administration) (at least at page 30, line 30 to page 31, line 10), teaches how to administer the compounds (at least at page 3, lines 10-31) and teaches which patients are in need of administration (at least at page 6, lines 26-29). Nothing more is legally required to enable the claims.

The examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. M.P.E.P. § 2164.04 (citing *In re Wright*, 999 F.2d 1557, 1562 (Fed. Cir. 1993)). In other words, it is incumbent upon the Patent Office, whenever a rejection on this basis is made, "to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." *Id.* Specific technical reasons are always required to support a *prima facie* case of lack of enablement. M.P.E.P. § 2164.04.

Applicants submit that pages 361-365 of the Carter *et al.* reference provided by the Examiner do not provide the requisite explanation and technical reasons as to why the Examiner would doubt the truth or accuracy of the present disclosure and, in fact,

actually demonstrate the broad spectrum of cancers that a compound can be active against. The Examiner has noted that only three compounds showed definite evidence of activity in the pancreas and only four in the colorectal and colon. However, Applicants point out that two of these compounds (*i.e.*, 5-FU and ADR) each showed activity in 15/23 cancers tested which demonstrates that certain compounds can and do have activity against a broad range of cancers.[1]

Indeed, in a non-precedential opinion of the Board of Patent Appeals and Interferences, a rejection under 35 U.S.C. § 112, first paragraph, for lack of enablement was reversed in a situation factually similar to the present case. *Ex Parte Bodian*, 1995 WL 1696869 (B.P.A.I. 1995). Briefly, the Board relied in part on *Fiers* in holding that the examiner failed to demonstrate a *prima facie* case of lack of enablement in connection with claims directed to methods of treating or preventing a viral condition because no evidence was provided to show that a person of ordinary skill could not practice the invention without undue experimentation. *Id.* As noted by the Board, the examiner has the burden of proof in establishing a *prima facie* case of lack of enablement which can only be met by providing such evidence. *Id.* Notably, the Board did not maintain a rejection of method of use claims, which encompassed the treatment of HIV, wherein the examiner supported the rejection by stating that there was no evidence of successful treatment of HIV. *Id.* In another similar case, the Federal Circuit's predecessor overturned a Board decision affirming a lack of enablement rejection to a claim directed to methods for treating lymphatic congestion despite the fact that the claim was construed to encompass many disease states *including cancer*. *Application of Sichert*, 566 F.2d 1154, 1160 (C.C.P.A. 1977) (emphasis added).[2]

Furthermore, the Federal Circuit has held that it is not necessary to enable one skilled in the art to make and use a perfected, commercially viable embodiment in order to satisfy the enablement requirement. *CFMT, Inc. v. Yieldup Int'l Corp.*, 349 F.3d 1333,

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[1] Applicants note that none of the compounds are described as inactive and that it is possible that the compounds tested were active *in vivo* or were active against the tested cell lines, but that the activity was not detectable by the methods used in Carter *et al.*, which was published almost 25 years ago. As the reference lacks an experimental section, Applicants cannot comment on the sensitivity of the methods used to acquire the data set forth in Carter *et al.*

[2] A copy of *Ex Parte Bodian* and *Application of Sichert* are enclosed for the Examiner's convenience.

1338 (Fed. Cir. 2003).[3] Indeed, an Applicant need not even demonstrate that an invention is completely safe to satisfy the requirements of 35 U.S.C. § 112. M.P.E.P. § 2164.01(c). The PTO should be wary not to overstep its role in examining patent applications. Indeed, the Federal Circuit has specifically stated that it is the Food and Drug Administration and not the PTO that determines the safety and efficacy of drugs for use in humans. *In re Brana*, 51 F.3d 1560, 1567 (Fed. Cir. 1995) (Testing for the full safety and effectiveness ... is more properly left to the Food and Drug Administration (FDA). Title 35 does not demand that such human testing occur within the confines of Patent and Trademark Office (PTO) proceedings). This regulatory process is not the same as the enablement requirement under 35 U.S.C. § 112.

The Examiner has stated that it would require undue experimentation to practice the claimed invention in part because of the need to determine an appropriate carrier, dosage, duration of treatment and route of administration. Applicants submit that physicians perform these tasks regularly every day. In fact, the Federal Circuit has held that a specification is enabling in part because those skilled in the art would know how to conduct a dose response study to determine the appropriate amounts to be used. *Merck & Co., Inc. v. Biocraft Laboratories, Inc.*, 874 F.2d 804, 809 (Fed. Cir. 1989).

The Examiner has further stated that it would require undue experimentation to practice the claimed invention in part because the compounds would have to be tested in an appropriate animal model. Applicants submit that there are numerous animal models known in the art for the various types of cancer. It is well established that the specification need not teach, and preferably omits, what is well know in the art. *Hybritech Inc. v. Monoclonal Antibodies*, 802 F.2d 1367,1385 (Fed. Cir. 1986). Furthermore, it is well established that the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 U.S.P.Q. 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, (Fed. Cir. 1985); M.P.E.P. § 2164.01. Accordingly, Applicants submit that practicing the claimed invention would not require undue experimentation.

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[3] Applicants note that the operability may be relevant to the enablement requirement. However, even assuming for the sake of argument that some of the compounds of the present claims are not effective against all claimed diseases, it is well-settled that the "presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled." M.P.E.P. § 2164.08(b).

Claims 22-24, 79, 83 and 84 have been canceled.

For the reasons set forth above, Applicants believe that the specification enables the remaining pending method claims directed to the treatment of cancer and, accordingly, that the rejection under 35 U.S.C. § 112, first paragraph, cannot stand and must be withdrawn.

II. The Rejection of Claims 50-69, 75-84, 86 and 87 Under 35 U.S.C. § 112, First Paragraph

Claims 50-69, 75-84, 86 and 87 have been rejected under 35 U.S.C. § 112, first paragraph, for allegedly not reasonably providing enablement for "preventing cancer."

Claims 51-54, 62-66 and 79-82 have been canceled without prejudice. Amended claims 50, 55-61, 67-69, 75-78, 83, 84, 86 and 87 do not recite the term "preventing."

Accordingly, Applicants submit that the rejection of claims 50-69, 75-84, 86 and 87 under 35 U.S.C. § 112, first paragraph, has been overcome and must be withdrawn.

III. The Rejection of Claims 22-24, 31-69, 75-84, 86 and 87 Under 35 U.S.C. § 102

Claims 22-24, 31-69, 75-84, 86 and 87 have been rejected under 35 U.S.C. § 102 for being allegedly anticipated by U.S. Patent Publication No. 2002/0161022 to Reich *et al.* ("Reich").

Claims 22-24, 31-34, 42-46, 51-54, 62-66, 79, 83 and 84 have been canceled without prejudice.

Claims 35, 39-41, 47, 48, 55, 59-61, 67, 68 and 78 have been amended to be in independent form. Applicants respectfully submit that the amended claims do not encompass any compound of Reich. Applicants note that these claims are commensurate in scope with the compound claims of U.S. application No. 09/910,950 (now U.S. Patent No. 6,897,231), of which the present application is a divisional application, which compounds have already been determined to be novel and non-obvious over Reich.

Accordingly, Applicants submit that the rejection of claims 22-24, 31-69, 75-84, 86 and 87 under 35 U.S.C. § 102 has been overcome and must be withdrawn.

IV. Previously Submitted Form PTO-1449 Listing References AA-BS

Applicants respectfully request that references AA-BS set forth in the Form PTO-1449 titled, "List of References Cited by Applicant," that was filed concurrently with the above-identified application on September 26, 2003, be made of record in the file history of the above-identified application by initialing the Form PTO-1449 and returning to Applicants.

Conclusion

Applicants respectfully request that the above remarks be entered in the present application file. No fee is believed to be due in connection with this Response other than that in connection with the Supplemental Information Disclosure Statement and Petition for Extension of Time; however, in the event that any additional fee is due, please charge the required fee to Jones Day Deposit Account No. 50-3013.

Respectfully submitted,

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Enclosures